Initial REMS with ETASU approval: 05/2011

NDA 21-071 AVANDIA (rosiglitazone maleate) Tablets
NDA 21-410 AVANDAMET (rosiglitazone maleate and metformin hydrochloride) Tablets
NDA 21-700 AVANDARYL (rosiglitazone maleate and glimepiride) Tablets

A thiazolidinedione agonist for peroxisome proliferator-activated receptor gamma

SmithKline Beecham (Cork) Ltd d/b/a GlaxoSmithKline Currabinny, Carrigaline, County Cork, Ireland

2301 Renaissance Boulevard Mail Code RN 0420 King of Prussia, PA 19406-2772

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

GOALS

The goals of the Avandia-Rosiglitazone Medicines Access Program (hereafter referred to as the Rosiglitazone REMS Program) are:

- 1. To restrict access to rosiglitazone-containing medicines (Avandia, Avandamet, Avandaryl) so that only prescribers who acknowledge the potential increased risk of myocardial infarction associated with the use of rosiglitazone are prescribing rosiglitazone.
- 2. To restrict access to patients who have been advised by a healthcare provider about the potential increased risk of myocardial infarction associated with the use of rosiglitazone and are one of the following:
 - either already taking rosiglitazone or
 - if not already taking rosiglitazone, they are unable to achieve glycemic control on other medications and, in consultation with their healthcare provider, have decided not to take pioglitazone for medical reasons

REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each rosiglitazone prescription in accordance with 21 CFR 208.24.

The Medication Guide for each product is part of the REMS and is appended.

B. Communication Plan

GlaxoSmithKline will implement a communication plan to support implementation of this REMS.

The communication plan will include:

- 1. Within 60 days of initial approval of the REMS, GlaxoSmithKline will send *Dear Pharmacist letters* to US pharmacists through mailings to pharmacies, long-term care facilities, and hospitals. The letter will include the following information:
 - purpose of the REMS program
 - potential for the increased risk of myocardial infarction associated with rosiglitazone use
 - description of the REMS
 - a statement of the need to transition current patients receiving rosiglitazone into the REMS program or place on alternate medicine
 - the date by which all patients must be transitioned into the REMS program or placed on alternative medicine and the date by which rosiglitazone will no longer be available through retail pharmacies
 - a description of the rosiglitazone distribution channel (i.e., through certified [mail order/specialty] pharmacies)
 - contact information for questions regarding the REMS
 - instructions for how pharmacies can return rosiglitazone medicines

The *Dear Pharmacist letter* is part of the REMS and is appended.

2. Within 60 days of initial approval of the REMS, a *Dear Healthcare Provider Letter* will be sent. The target audience for the letter will include prescribers who have written a prescription for rosiglitazone within the year prior to initial approval of the REMS. The letter will include a copy of the Full Prescribing Information and Medication Guides for each rosiglitazone product and will be available on the Rosiglitazone REMS program website for 6 months from the date of issuance of the letter.

The following REMS materials will be included with the *Dear Healthcare Provider Letter*.

- a) Prescriber Overview
- b) Prescriber Enrollment Form
- c) Patient Enrollment Form
- d) Medication Guides

The *Dear Healthcare Provider Letter* is part of the Rosiglitazone REMS Program and is appended.

All communication materials will be available in electronic format beginning no later than 60 days after initial approval of the REMS and continuing for six months after initial approval of the REMS via the REMS program website (www.Avandia.com) as well as in print format.

C. Elements to Assure Safe Use

Healthcare providers who prescribe rosiglitazone-containing medicines for outpatient or long-term care use are specially certified

- a. GlaxoSmithKline will ensure healthcare providers who prescribe rosiglitazone for outpatient or long-term care use are specially certified. GlaxoSmithKline will begin enrolling prescribers no later than 60 days after initial approval of the REMS.
- b. To become specially certified to prescribe rosiglitazone, prescribers will be required to enroll in the Rosiglitazone REMS Program and must:
 - 1) Review the Rosiglitazone REMS *Prescriber Overview* and the Full Prescribing Information, including the *Medication Guide*.
 - 2) Complete and sign the *Prescriber Enrollment Form* and submit it to the Rosiglitazone REMS Program.
 - 3) Agree to complete and sign a Rosiglitazone REMS *Patient Enrollment Form* for each patient enrolled.
 - 4) Agree to provide and review the *Medication Guide* for the prescribed rosiglitazone medicine with the patient or caregiver.
 - 5) Agree to provide a completed, signed copy of the *Patient Enrollment Form* to the patient, retain a copy for my records, and submit a copy to the Rosiglitazone REMS Program.
- c. GlaxoSmithKline will inform enrolled prescribers following substantial changes to the Rosiglitazone REMS or REMS Program. Substantial changes include: 1) significant changes to the operation of the Program or 2) Changes to the Prescribing Information and Medication Guide that affect the risk-benefit profile of rosiglitazone.

d. GlaxoSmithKline will:

1) Ensure that prescriber enrollment can be completed via the *Rosiglitazone REMS Program website*, by phone, or by faxing the forms.

The website is part of the Rosiglitazone REMS Program and is appended.

- 2) Ensure that, as part of the enrollment process, prescribers receive the following materials that are part of the Rosiglitazone REMS
 - a) Prescriber Overview
 - b) Prescriber Enrollment Form
 - c) Patient Enrollment Form
 - d) Medication Guide

- 3) Ensure that the *Prescriber Enrollment Form* is complete before activating a prescriber's enrollment in the REMS Program
- 4) Ensure that prescribers are notified when they have been successfully enrolled in the Rosiglitazone REMS program, and therefore, certified to prescribe rosiglitazone.

2. Rosiglitazone will be dispensed only by specially certified pharmacies.

GlaxoSmithKline will ensure that rosiglitazone will only be dispensed by certified pharmacies. To become certified to dispense rosiglitazones, each pharmacy must be enrolled in the Rosiglitazone REMS Program.

To be certified, the pharmacy must agree to the following:

- a. To have a system in place to be able to verify that the prescriber (if the prescriber has prescribed rosiglitazone for outpatient or long-term care use) and patient are enrolled in the Rosiglitazone REMS Program prior to dispensing each time rosiglitazone is prescribed. If the patient and prescriber are not enrolled, rosiglitazone cannot be dispensed.
- b. To educate all pharmacy staff involved in the dispensing of rosiglitazone on the program requirements of the REMS.
- c. To provide a Medication Guide each time rosiglitazone is dispensed.
- d. To be audited to ensure that all processes and procedures are in place and are being followed for the Rosiglitazone REMS.

3. Rosiglitazone will only be dispensed to patients with evidence or other documentation of safe-use conditions

GlaxoSmithKline will ensure that rosiglitazone will only be dispensed if there is documentation in the Rosiglitazone REMS Program system that the dispensing pharmacy, prescriber (if the prescriber will prescribe rosiglitazone for outpatient or long-term care use), and patient are all enrolled in the Program. To become enrolled, each patient must review the Medication Guide and sign the *Patient Enrollment Form* with their prescriber.

The *Patient Enrollment Form* is part of the REMS and is appended.

D. Implementation System

- 1. GlaxoSmithKline will ensure that pharmacies (including pharmacy distributors) dispensing rosiglitazone are specially certified using the criteria described above.
- 2. GlaxoSmithKline will ensure that distributors who distribute rosiglitazone are specially certified. Specially certified distributors will agree to:

- a. Distribute rosiglitazone medicines only to pharmacies certified in the Rosiglitazone REMS Program. In the case of patients in longterm care facilities or hospitals, specially certified distributors will provide rosiglitazone on a named patient basis.
- b. Put processes and procedures in place to ensure that the requirements of the Rosiglitazone REMS are followed.
- c. Be audited to ensure that rosiglitazone medicines are distributed according to the REMS
- 3. GlaxoSmithKline will ensure that all rosiglitazone medicines are withdrawn from uncertified pharmacies within 6 months after the initial approval of the REMS. GlaxoSmithKline will monitor distribution of rosiglitazone to check that these products are being shipped only to certified pharmacies. GlaxoSmithKline will ensure that noncertified distributors and pharmacies are sent an *Urgent Drug Withdrawal letter* instructing them to immediately return product.

The *Urgent Drug Withdrawal letter* is part of the REMS and is appended.

- 4. GlaxoSmithKline will maintain a secure, validated, interactive, web-based database of all enrolled entities (prescribers, pharmacies, patients, and distributors). The database allows certified prescribers to enroll themselves and to enroll patients. Certified pharmacies can access the database to verify patient and prescriber enrollment status as required by the REMS, and dispense rosiglitazone for enrolled patients based on an electronic or written prescription. GlaxoSmithKline will monitor and evaluate implementation of the Rosiglitazone REMS requirements.
- 5. GlaxoSmithKline will monitor distribution data and prescription data to ensure that only enrolled distributors are distributing, enrolled pharmacies are dispensing, and enrolled prescribers (who prescribe rosiglitazone for outpatient or long-term care use) are prescribing rosiglitazone. Additionally GlaxoSmithKline will monitor to ensure that rosiglitazone is only being dispensed to enrolled patients. Corrective action will be instituted by GlaxoSmithKline if noncompliance is found.
 - a. Patients in inpatient facilities will be shipped drug per patient if the patient is enrolled in the REMS program
 - b. Patients in long-term care facilities and patients prescribed rosiglitazone for outpatient use will be shipped drug per patient if the patient and the prescriber are enrolled in the REMS Program
- 6. GlaxoSmithKline will monitor and audit the distribution and dispensing systems to check that all processes and procedures are in place and functioning to support the requirements of the Rosiglitazone REMS.
- 7. GlaxoSmithKline will maintain a Program Coordinating Center with a Call Center to support patients, prescribers, pharmacies, and distributors in interfacing with the REMS. GlaxoSmithKline will ensure that all materials listed in or appended to the Rosiglitazone Medicines Access REMS Program will be available through the REMS Program website (www.Avandia.com) or by calling the Call Center at 1-800 Avandia.

- 8. If there are substantive changes to the Rosiglitazone REMS or REMS Program, GlaxoSmithKline will update all affected materials and notify enrolled pharmacies, prescribers, distributors, and patients of the changes, as applicable. Notification for patients will be sent to the patient's prescriber. Substantive changes are defined as:
 - a. Significant changes to the operation of the Rosiglitazone REMS or REMS Program, or
 - b. Changes to the Prescribing Information and Medication Guide that affect the risk-benefit profile of rosiglitazone.
- 9. Based on monitoring and evaluation of these elements to assure safe use, GlaxoSmithKline will take reasonable steps to improve implementation of these elements and to maintain compliance with the Rosiglitazone REMS requirements, as applicable.
- 10. GlaxoSmithKline will develop and follow written procedures and scripts to implement the REMS.

E. Timetable for Submission of Assessments

GlaxoSmithKline will submit REMS assessments to FDA 6 months, 12 months, and annually from [insert the date of initial approval of this REMS]. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. GlaxoSmithKline will submit each assessment so that it will be received by the FDA on or before the due date.



[DATE, 2011]

GlaxoSmithKline
2301 Renaissance Boulevard
P.O. Box 61540
King of Prussia, PA
19406-2772

IMPORTANT DRUG WARNING

Subject: Rosiglitazone Medicines: Potential Increased Risk of Myocardial Infarction

FDA-Mandated Restricted Distribution Program

Dear Healthcare Provider,

GlaxoSmithKline (GSK) is informing you about the Avandia-Rosiglitazone Medicines Access Program, hereafter referred to as the Rosiglitazone Risk Evaluation and Mitigation Strategy (REMS) Program. This restricted access and dispensing program has been required by the Food and Drug Administration (FDA) for rosiglitazone medicines [i.e., Avandia (rosiglitazone maleate), Avandamet (rosiglitazone maleate/metformin hydrochloride), and Avandaryl (rosiglitazone maleate/glimepiride)] to ensure that the benefits of the drugs outweigh the potential increased risk of myocardial infarction associated with their use. Prescribers and patients must enroll in the Rosiglitazone REMS Program in order for prescribers to be able to prescribe and patients to be able to receive rosiglitazone medicines. After [Approval Date + 6 months], patients will no longer be able to obtain their rosiglitazone medicines from their local pharmacies, but will have to receive them by mail from one of the specially certified pharmacies participating in the Rosiglitazone REMS Program.

The Rosiglitazone REMS limits the use of rosiglitazone to:

- Patients already taking rosiglitazone, who have been advised by a healthcare professional of the risks and benefits of rosiglitazone, including the potential increased risk of myocardial infarction, or
- Patients not already taking rosiglitazone who: (1) are unable to achieve adequate glycemic control
 on other diabetes medications, and (2) have been advised of the risks and benefits of rosiglitazone,
 including the potential increased risk of myocardial infarction, and (3) in consultation with their
 healthcare provider, have decided not to take pioglitazone (ACTOS®) for medical reasons.

Rosiglitazone is not recommended in patients with symptomatic heart failure.

Potential Risk of Myocardial Infarction

A meta-analysis of 52 clinical trials (mean duration 6 months; 16,995 total patients), most of which compared Avandia to placebo, showed Avandia to be associated with a statistically significant increased risk of myocardial infarction. Three other trials (mean duration 46 months; 14,067 total patients), comparing Avandia to some other approved oral antidiabetic agents or placebo, showed a statistically non-significant increased risk of myocardial infarction, and a statistically non-significant decreased risk of death. There have been no clinical trials directly comparing cardiovascular risk of Avandia and ACTOS (pioglitazone, another thiazolidinedione), but in a separate trial, pioglitazone (when compared to placebo) did not show an increased risk of myocardial infarction or death.

Healthcare Provider Responsibilities for Participation in the Rosiglitazone REMS Program

As a healthcare provider, you must be enrolled in the Rosiglitazone REMS Program in order to prescribe rosiglitazone. As part of this program, you will be educated about the potential increased risk of myocardial infarction and the need to limit the use of rosiglitazone to eligible patients. You will also be required to complete a Prescriber Enrollment Form.

Once you are enrolled, then you can enroll eligible patients into the Rosiglitazone REMS Program. <u>You must enroll your patients in the program in order for them to begin or continue to receive rosiglitazone medicines.</u>

Transition of Current Patients

You will need to discuss with patients the risks and benefits of taking rosiglitazone. After [Approval Date + 6 months], patients will no longer be able to obtain their rosiglitazone medicines from their local pharmacies. It is important that you contact patients currently taking rosiglitazone as soon as possible so that they are able to maintain access to their medication. To enroll a patient in the Rosiglitazone REMS Program both you and your patient will need to complete the Patient Enrollment Form. You will also need to complete the Prescription Information section of the Patient Enrollment Form so that your patient can be dispensed rosiglitazone through the restricted dispensing system. Once patients are enrolled in the REMS Program, they will be receiving their rosiglitazone medicine by mail from one of the specially certified pharmacies in the Rosiglitazone REMS Program.

Enclosed Materials for Enrollment in the Rosiglitazone REMS Program

The following materials are enclosed:

- Prescriber Overview
- Prescriber Enrollment Form (this is a one-time only requirement)
- Patient Enrollment Forms (this is a one-time only requirement)
- · Patient Medication Guides

You can enroll either on-line, by phone, or by fax and you can enroll your patients either on-line, or by fax.

Additional copies of the Program materials are available through the Program website (www.avandia.com) or by faxing or calling the Rosiglitazone REMS Coordinating Center. For all questions concerning the Program, please contact the Coordinating Center at:

Phone: 1-800-AVANDIA (1-800-282-6342)

Fax: 1-888-772-9404

Coordinating Center hours of operation: Monday through Friday from 8:00AM to 8:00PM ET.

Please see accompanying complete prescribing information, including the BOXED WARNING and WARNINGS and PRECAUTIONS sections; and Medication Guides, for Avanda, Avandamet, and Avandaryl.

Sincerely,

Alexander R. Cobitz, MD, PhD
Director, Cardiovascular and Metabolism
Medical Development Center
GlaxoSmithKline Pharmaceuticals



[DATE, 2011]

GlaxoSmithKline 2301 Renaissance Boulevard P.O. Box 61540 King of Prussia, PA 19406-2772

IMPORTANT DRUG WARNING

Subject: Rosiglitazone Medicines: Potential Increased Risk of Myocardial Infarction;

Withdrawal of Rosiglitazone Medicines from Current Supply Chain

Effective XX/ 2011

Dear Pharmacist,

GlaxoSmithKline (GSK) is informing you about the Avandia-Rosiglitazone Medicines Access Program, hereafter referred to as the Rosiglitazone Risk Evaluation and Mitigation Strategy (REMS). This restricted access and dispensing program has been required by the Food and Drug Administration (FDA) for rosiglitazone medicines [i.e., Avandia (rosiglitazone maleate), Avandamet (rosiglitazone maleate/metformin hydrochloride), and Avandaryl (rosiglitazone maleate/glimepiride)] to ensure that the benefits of the drugs outweigh the potential increased risk of myocardial infarction associated with their use. Prescribers and patients must enroll in the Rosiglitazone REMS Program in order for prescribers to be able to prescribe and patients to be able to receive rosiglitazone medicines. Rosiglitazone medicines will only be available through specially certified pharmacies.

The Rosiglitazone REMS limits the use of rosiglitazone to:

- Patients already taking rosiglitazone, who have been advised by a healthcare professional of the risks and benefits of rosiglitazone, including the potential increased risk of myocardial infarction, or
- Patients not already taking rosiglitazone who are: (1) unable to achieve adequate glycemic control on other diabetes medications, and (2) have been advised of the risks and benefits of rosiglitazone, including the potential increased risk of myocardial infarction, and (3) in consultation with their healthcare provider, have decided not to take pioglitazone (ACTOS®) for medical reasons.

Rosiglitazone is not recommended in patients with symptomatic heart failure.

Effective [Approval Date + 6 months], GSK will withdraw rosiglitazone medicines from the current supply chain. Therefore, patients prescribed rosiglitazone medicines will no longer be able to have their prescriptions filled at your pharmacy. It is important that you advise any patients filling a prescription at your pharmacy to contact their physician as soon as possible in order to determine if they are appropriate for enrollment in the Rosiglitazone REMS Program. Their physician will discuss the risks and benefits of rosiglitazone medicines, including the potential increased risk of myocardial infarction, and if appropriate, will complete the necessary Rosiglitazone REMS enrollment materials.

You will receive a second communication with instructions on returning rosiglitazone medicines to GSK c/o Stericycle [Date=1 month prior to end of transition period].

Potential Increased Risk of Myocardial Infarction

A meta-analysis of 52 clinical trials (mean duration 6 months; 16,995 total patients), most of which compared AVANDIA to placebo, showed AVANDIA to be associated with a statistically significant increased risk of myocardial infarction. Three other trials (mean duration 46 months; 14,067 total patients), comparing AVANDIA to some other approved oral antidiabetic agents or placebo, showed a statistically non-significant increased risk of myocardial infarction, and a statistically non-significant decreased risk of death. There have been no clinical trials directly comparing cardiovascular risk of AVANDIA and ACTOS (pioglitazone, another thiazolidinedione), but in a separate trial, pioglitazone (when compared to placebo) did not show an increased risk of myocardial infarction or death.

Please see accompanying complete prescribing information, including the BOXED WARNING and WARNINGS and PRECAUTIONS sections; and Medication Guides, for Avanda, Avandamet, and Avandaryl.

If you have any questions regarding the Rosiglitazone REMS Program, please call 1-800-AVANDIA or visit the Rosiglitazone REMS website [www.AVANDIA.com]. The Coordinating Center hours of operation are Monday through Friday from 8:00AM to 8:00PM ET.

Sincerely,

Alexander R. Cobitz, MD, PhD
Director, Cardiovascular and Metabolism
Medical Development Center
GlaxoSmithKline Pharmaceuticals



Prescriber Program Overview

The Avandia-Rosiglitazone Medicines Access Program (hereafter referred to as the Rosiglitazone Risk Evaluation and Mitigation Strategy [REMS] Program) is being required by the Food and Drug Administration (FDA) for rosiglitazone medicines [i.e., Avandia (rosiglitazone maleate), Avandamet (rosiglitazone maleate/metformin hydrochloride), and Avandaryl (rosiglitazone maleate/glimepiride) to ensure that the benefits of the drugs outweigh the potential increased risk of myocardial infarction associated with their use. This program restricts the availability of rosiglitazone medicines to healthcare providers and patients who are enrolled in the Program. As part of the Rosiglitazone REMS, prescribers are educated about this potential risk and the need to limit the use of rosiglitazone medicines to certain patients.

The Rosiglitazone REMS limits the use of rosiglitazone medicines to

- Patients already taking rosiglitazone, who have been advised by a healthcare professional of the risks and benefits of rosiglitazone, including the potential increased risk of myocardial infarction, or
- Patients not already taking rosiglitazone who are: (1) unable to achieve adequate glycemic control on other diabetes medications, and (2) have been advised of the risks and benefits of rosiglitazone, including the potential increased risk of myocardial infarction, and, (3) in consultation with their healthcare provider, have decided not to take pioglitazone (ACTOS®) for medical reasons.

Both prescribers and patients must enroll in the Rosiglitazone REMS Program in order to be able to access rosiglitazone medicines.

Steps to Prescriber Enrollment

- 1. Review the Prescriber Overview (included in this brochure).
- 2. Complete the Prescriber Enrollment Form.
- 3. Submit the Prescriber Enrollment Form to the Coordinating Center either online, over the phone, or by fax.

An enrollment confirmation will be sent to you by e-mail.

You may designate an office contact to assist with data entry activities and any potential communications between your office and the Coordinating Center.

You and your office contact will each receive a username and password to access the web-based system for online patient enrollment.

Once you are enrolled, you can enroll eligible patients into the Rosiglitazone REMS Program.

Steps to Enroll a Patient

Phone: 1-800-AVANDIA

- 1. Determine that the patient is an appropriate candidate for treatment with rosiglitazone.
- 2. Educate patients on the risks and benefits of taking rosiglitazone, and provide them with a Medication Guide. Encourage them to ask questions about rosiglitazone.
- 3. Answer the questions your patient may have about rosiglitazone and the Rosiglitazone REMS.
- 4. Review and complete the Patient Enrollment Form with your patient. Be sure that you both sign the form. Be sure to complete the Prescription Information section of the Patient Enrollment Form. Provide the patient with a copy of the signed Patient Enrollment Form.
- 5. Either fax the completed Patient Enrollment Form to the Rosiglitazone REMS Coordinating Center or log on to the online system and complete the Patient Enrollment Form. Either fax the prescription and insurance information or attach this information as prompted during online enrollment.
- 6. Once the Rosiglitazone REMS Program processes the Patient Enrollment Form, the prescription will be submitted to a specially certified mail order pharmacy for dispensing.
- The patient will receive the rosiglitazone medicine by mail from the mail order pharmacy. Rosiglitazone medicines will not be available through retail pharmacies.







The Rosiglitazone REMS limits the use of rosiglitazone medicines. After consultation with a healthcare professional who has considered and advised the patient of the risks and benefits of rosiglitazone, this drug may be prescribed to:

- · Patients already taking a rosiglitazone or
- Patients not already taking rosiglitazone who are unable to achieve glycemic control on other medications, and in consultation with their healthcare provider, have decided not to take pioglitazone (ACTOS) for medical reasons.

Rosiglitazone is not recommended in patients with symptomatic heart failure.

Boxed Warning

Potential Risk of Myocardial Infarction

A meta-analysis of 52 clinical trials (mean duration 6 months; 16,995 total patients), most of which compared AVANDIA to placebo, showed AVANDIA to be associated with a statistically significant increased risk of myocardial infarction. Three other trials (mean duration 46 months; 14,067 total patients), comparing AVANDIA to some other approved oral antidiabetic agents or placebo, showed a statistically non-significant increased risk of myocardial infarction, and a statistically non-significant decreased risk of death. There have been no clinical trials directly comparing cardiovascular risk of AVANDIA and ACTOS (pioglitazone, another thiazolidinedione), but in a separate trial, pioglitazone (when compared to placebo) did not show an increased risk of myocardial infarction or death.

For Your Patients Currently Being Treated With Rosiglitazone

You must inform each of your patients currently receiving rosiglitazone of the product's risk information, including the current state of knowledge about the potential increased risk of myocardial infarction associated with the use of rosiglitazone. Also inform patients that pioglitazone (ACTOS) has not been shown to be associated with an increased risk of myocardial infarction. You must document in the patient's medical record that the patient received the Medication Guide and acknowledged understanding of the risk information.

For Your Patients Not Currently Taking Rosiglitazone

Before starting a new patient on rosiglitazone, you must determine that they are unable to achieve glycemic control on other diabetes medications, and (in consultation with you), that they have decided not to take pioglitazone (ACTOS) for medical reasons. You must inform them of the product's risk information, including the current state of knowledge about the potential increased risk of myocardial infarction associated with the use of rosiglitazone. Also inform them that pioglitazone (ACTOS) has not been shown to be associated with an increased risk of myocardial infarction. You must document in the patient's medical record that the patient has received the Medication Guide and acknowledged understanding of the risk information.

Review the Complete Prescribing Information for Avandia[®], Avandamet[®], and Avandaryl[®].

Additional copies of the Program materials are available through the Program website or by faxing or calling the Rosiglitazone REMS Coordinating Center. Please contact the Coordinating Center with questions regarding the Rosiglitazone REMS.

Phone: 1-800-AVANDIA (1-800-282-6342)

Fax: 1-888-772-9404 www.AVANDIA.com

Phone: 1-800-AVANDIA

Coordinating Center hours of operation: Monday through Friday from 8:00 AM to 8:00 PM ET







Prescriber Enrollment Form (Please Print) *indicates required fields

This Prescriber Enrollment Form must be completed before you can prescribe rosiglitazone medicines, including:

- Avandia® (rosiglitazone maleate) Tablets,
- Avandamet® (rosiglitazone maleate and metformin hydrochloride) Tablets, and
- Avandaryl® (rosiglitazone maleate and glimepiride) Tablets.

These medicines are only available through the Rosiglitazone REMS Program.

	Prescriber Information *First Name:						*Last Name:		
	*Credentials:		00 🗆 1	IP 🗆 PA	□ Othe	er			
	*Specialty:						Cardiology		
		☐ Primary Car	e/Family Pra	actice/Gener	al Practice		Other		
	Name of Facility:								
	*Address 1:								
œ	Address 2:								
PRESCRIBER	*City:				*State:		*Zipcode:		
	*Phone Number:			_ *Fax Number:					
	*Email:								
	*National Provider Identification (NPI) Number:								
	or								
	*State License Number:			*State of Issue:					
	Office Contact Information								
	First Name:				L	Last Name:			
	Phone Number:				F	ax Nur	nber:		
	(if different from above)				(if different from above)				
	*Email (If Office Co	ontact is provided) : .							









Prescriber Agreement

By signing below, I agree to comply with the following REMS requirements:

- I have read the Rosiglitazone REMS Prescriber Overview and the Full Prescribing Information.
- I understand that rosiglitazone may be associated with an increased risk of myocardial infarction, and this is the reason that this Program is necessary.
- I understand that only patients who meet one of the following criteria are eligible to receive rosiglitazone:
 - Patients currently taking rosiglitazone who have been advised by me of the risks and benefits of rosiglitazone, including the potential
 increased risk of myocardial infarction, and have acknowledged that they understand the potential risk, and have agreed to enroll in the
 REMS Program.
 - Patients not currently taking rosiglitazone who are unable to achieve glycemic control on other medications, have acknowledged that they
 understand the potential increased risk of myocardial infarction associated with the use of rosiglitazone, and in consultation with me, have
 decided not to take the alternative medication pioglitazone (ACTOS®) for medical reasons, and have agreed to enroll in the REMS Program.
- After obtaining the patient's or caregiver's signature, I will complete and sign a Rosiglitazone REMS Patient Enrollment Form for each patient
 enrolled and submit it to the Rosiglitazone REMS Program.
- In signing, the Patient Enrollment Form, I document the patient is eligible to receive rosiglitazone because he/she meets the criteria in one of the
 two categories listed above. The Medication Guide for the prescribed rosiglitazone medicine has been provided to and reviewed with the patient
 or caregiver.
- The patient has acknowledged understanding about the potential increased risk of myocardial infarction associated with the use of rosiglitazone.
- I will provide a completed, signed copy of the Patient Enrollment Form to the patient, and retain a copy for my records. I will also provide a completed signed copy or verification that I have obtained the patient's signature (for online enrollment) to the Rosiglitazone REMS Program. I understand the pharmacy cannot dispense a rosiglitazone medicine without this documentation.
- I understand that if I fail to maintain compliance with the requirements of the Rosiglitazone REMS Program, I will no longer be able to participate in the Program, and therefore will not be able to prescribe rosiglitazone.
- I may provide an office contact to assist with data entry activities and any potential communications between my office and the Rosiglitazone REMS Program. My office contact and I will receive a user name and password to access the web-based system for online patient enrollment into the Rosiglitazone REMS Program.
- I understand that the Rosiglitazone REMS Program may contact me to resolve discrepancies, to obtain information about a patient, or to provide other information related to the Rosiglitazone REMS Program.

*Prescriber Signature: *Date	(MM/DD/YY) :
------------------------------	---------------------

I may cancel this enrollment by notifying the Rosiglitazone REMS Program by fax at 1-888-772-9404 or by phone at 1-800-282-6342. The Rosiglitazone REMS Program may dis-enroll prescribers who are not compliant with the Program requirements.









Phone: 1-800-AVANDIA Fax: 1-888-772-9404 www.AVANDIA.com

Patient Enrollment Form (Please Print) *indicates required fields					
	•		-	*DOB (MM/DD/YY):	
me cal	dicine. Rosiglitazone medicines are availa	ble only d Mitigat	through the Avandia-Ros ion Strategy (REMS) Progr	althcare provider before you can receive a rosiglitazone iglitazone Medicines Access Program, hereafter ram. You will not be able to get your medicine at your	
	ese medicines contain rosiglitazone:				
•	Avandia® (rosiglitazone maleate)	l	nin hudusahlarida)		
•	Avandamet® (rosiglitazone maleate and		,		
•	Avandaryl® (rosiglitazone maleate and	giimepiri	ae)		
Pat	ient Agreement				
Вуз	signing this form, I agree that:				
•	I have read and talked with my doctor or heal for me.	thcare pro	vider about the risk information	in the Medication Guide for the rosiglitazone medicine prescribed	
•	•	me about	the risks associated with alter	t with me, including that these medicines may increase my risk of native medicines containing pioglitazone (ACTOS®), which has not	
•	I have had enough time with my doctor or hea about rosiglitazone medicines or my diabetes			to ask him or her questions and talk about any concerns I have	
•	I understand that to get a rosiglitazone medici	ne, I have	to enroll in the Rosiglitazone R	EMS Program.	
•	I understand that the Rosiglitazone REMS Prog Rosiglitazone REMS Program.	gram may	contact me by phone, mail or e	email for more information about my taking part in the	
•	Program established by GlaxoSmithKline (GSK) and to th , and my r	ne Rosiglitazone REMS Program name, address, and telephone n	ner "my Providers") participating in the Rosiglitazone REMS n Coordinating Center to share my personally identifiable health umber (together my "Protected Health Information") for the and managing the Program.	
•	Lunderstand that all information collected on	the enrolln	nent form will he stored in a se	cure database maintained by the Coordinating Center	



After joining the program, if you do not get your first prescription within about two weeks, call your health care provider or the Rosiglitazone REMS Program at

Printed Name of Guardian:_

1-800-AVANDIA (1-800-282-6342).









Phone: 1-800-AVANDIA Fax: 1-888-772-9404 www.AVANDIA.com

Patient Enrollment Form (Please Print) *indicates required fields

	Patient Information						
	*First Name: MI:*Last Name:						
	*Date of Birth (MM/DD/YY): *Gender: □ Female □ Male						
	*Address 1:						
FZ	Address 2:						
PATIENT	*City:*State:*Zipcode:						
Ť	*Phone:Alternate Phone:						
	Email:						
	*Do you have insurance: YES □ NO □						
	*Is the patient: □ new to rosiglitazone therapy □ continuing rosiglitazone therapy						
	Fax all patient insurance information, including drug benefit cards (front and back) with this enrollment form to 1-888-772-9404.						
	Prescriber Information						
۲r	*First Name: MI:*Last Name:						
PRESCRIBER	*National Provider Identification (NPI) Number:						
CR	Or .						
RES	*State License Number:*State of Issue:						
<u>a</u>	Name of Facility (if applicable):						
	*Phone Number:						
-	Prescription Information (to be completed by your doctor or other healthcare provider):						
N O	Prescription: Avandia®						
IPTI	□ Avandamet®						
PRESCRIPTION	☐ Avandaryl®						
PRE	Provide Dosing Instructions:						
	Number of refills:						
_	By signing this form, I acknowledge that I have discussed the risk information with this patient. I have documented in his/her medical record that this patient meets the eligibility criteria for enrollment into the Rosiglitazone REMS Program.						
Pres	Prescriber Signature:*Date (MM/DD/YY):						
	Printed Name of Prescriber:						

Please fax the completed form to 1-888-772-9404 and provide a copy of this from to the patient.









Phone: 1-800-AVANDIA Fax: 1-888-772-9404



GlaxoSmithKline

2301 Renaissance Boulevard P.O. Box 61540 King of Prussia, PA 19406-2772

URGENT: DRUG WITHDRAWAL FROM PHARMACIES NOT ENROLLED IN RESTRICTED ACCESS PROGRAM

Date 2011 Event: XXXX

Re: Withdrawal of Rosiglitazone Medicines from pharmacies not enrolled in restricted

access program-

AVANDIA® (rosiglitazone maleate) Tablets AVANDAMET® (rosiglitazone maleate and metformin hydrochloride) Tablets AVANDARYL® (rosiglitazone maleate and glimepiride) Tablets

Dear Customer:

GlaxoSmithKline has implemented a restricted access and dispensing system for all rosiglitazone medicines (i.e., the Avandia-Rosiglitazone Medicines Access Program also referred to as the Rosiglitazone Risk Evaluation and Mitigation Strategy (REMS)) because of the potential increased risk of myocardial infarction associated with the use of rosiglitazone medicines. As part of the implementation of the program, GlaxoSmithKline is withdrawing these products from wholesalers and pharmacies that are not part of the restricted dispensing system. Rosiglitazone medicines are sold in the following presentation.

Product Description	NDC	Package Size
AVANDIA® (rosiglitazone maleate) Tablets 2 mg	0029-3158-18	Bottles of 60
AVANDIA® (rosiglitazone maleate) Tablets 4 mg	0029-3159-13	Bottles of 30
AVANDIA® (rosiglitazone maleate) Tablets 4 mg	0029-3159-00	Bottles of 90
AVANDIA® (rosiglitazone maleate) Tablets 8 mg	0029-3160-13	Bottles of 30
AVANDIA® (rosiglitazone maleate) Tablets 8 mg	0029-3160-59	Bottles of 90
AVANDAMET® (rosiglitazone maleate and metformin HCL) Tablets 2 mg/1000 mg	0007-3163-18	Bottles of 60

Product Description	NDC	Package Size
AVANDAMET® (rosiglitazone maleate and metformin HCL) Tablets 2 mg/500 mg	0007-3167-18	Bottles of 60
AVANDAMET® (rosiglitazone maleate and metformin HCL) Tablets 4 mg/1000 mg	0007-3164-18	Bottles of 60
AVANDAMET® (rosiglitazone maleate and metformin HCL) Tablets 4 mg/500 mg	0007-3168-18	Bottles of 60
AVANDARYL® (rosiglitazone maleate and glimepiride) Tablets 4 mg/2 mg	0007-3152-13	Bottles of 30
AVANDARYL® (rosiglitazone maleate and glimepiride) Tablets 4 mg/4 mg	0007-3153-13	Bottles of 30
AVANDARYL® (rosiglitazone maleate and glimepiride) Tablets 8 mg/2 mg	0007-3148-13	Bottles of 30
AVANDARYL® (rosiglitazone maleate and glimepiride) Tablets 8 mg/4 mg	0007-3149-13	Bottles of 30

Please examine your inventory immediately and return all units of the listed rosiglitazone medicines to GlaxoSmithKline, c/o Stericycle, 2670 Executive Drive, Suite A, Indianapolis, IN 46241. Stop distributing and immediately quarantine all listed rosiglitazone medicines. Please carry out a physical count and record this data on the business reply card and the packing slip which are included with this letter. It is very important that you complete the requested information on the enclosed postage paid Business Reply Card and return it to us within five (5) business days, even if you do not have the listed rosiglitazone medicines in stock.

Thank you for your cooperation. For shipping assistance or questions about the withdrawal process, please contact Stericycle at 1-866-324-3735 (TBC). A check will be issued for the price in effect at the time of purchase. In addition, a service and handling charge will be included based on HDMA guidelines. If you have any medical questions, please contact the GlaxoSmithKline Response Center at 1-888-825-5249 between 8:00 a.m. and 6:00 p.m. ET, Monday through Friday.

This withdrawal is being conducted with the knowledge of the Food and Drug Administration (FDA). We appreciate your immediate attention and cooperation.

Enclosures: Postage Paid Business Reply Card

Packing Slip and Prepaid UPS Return Service Shipping Label

Welcome to the Avandia-Rosiglitazone Medicines Access Program

Avandia-Rosiglitazone Medicines Access Program™

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

LOG IN

Prescribing Information

Medication Guide

For more information about the Avandia-Rosiglitazone Medicines Access Program, please tell us who you are:



I am a Patient



I am a Prescriber



I am a Pharmacist







Complete Prescribing Information, including Boxed WARNING and Medication Guide, for AVANDIA, AVANDAMET, and AVANDARYL.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase your risk of a heart attack (myocardial infarction). This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

600 pixel line

For more information about AVANDIA, please see Medication Guide and full Prescribing Information, including Boxed WARNING.

For more information about AVANDAMET, please see Medication Guide and full Prescribing Information, including Boxed WARNING.

For more information about AVANDARYL, please see Medication Guide and full Prescribing Information, including Boxed WARNING.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline.
This section is intended for U.S. residents only.
© 2011 GlaxoSmithKline. All Rights Reserved.

Avandia-Rosiglitazone Medicines Access Program Prescriber Overview

Avandia-Rosiglitazone Medicines Access Program™

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

LOG IN

Home

Prescribing Information

Medication Guide

The Avandia-Rosiglitazone Medicines Access Program is being required by the Food and Drug Administration (FDA) for rosiglitazone medicines [i.e., Avandia (rosiglitazone maleate), Avandamet (rosiglitazone maleate/metformin hydrochloride), and Avandaryl (rosiglitazone maleate/glimepiride) to ensure that the benefits of the drugs outweigh the potential increased risk of myocardial infarction associated with their use. This program restricts the availability of rosiglitazone medicines to healthcare providers and patients who are enrolled in the Program. As part of the Avandia-Rosiglitazone Medicines Access Program, prescribers are educated about this potential risk and the need to limit the use of rosiglitazone medicines to certain patients.

The Avandia-Rosiglitazone Medicines Access Program limits the use of rosiglitazone medicines to

- Patients already taking rosiglitazone, who have been advised by a healthcare professional of the risks and benefits of rosiglitazone, including the potential increased risk of myocardial infarction, or
- Patients not already taking rosiglitazone who are: (1) unable to achieve adequate glycemic control on other diabetes
 medications, and (2) have been advised of the risks and benefits of rosiglitazone, including the potential increased risk of
 myocardial infarction, and, (3) in consultation with their healthcare provider, have decided not to take pioglitazone (ACTOS®) for
 medical reasons.

Both prescribers and patients must enroll in the Avandia-Rosiglitazone Medicines Access Program in order to be able to access rosiglitazone medicines.

Dear Healthcare Professional Letter

600 pixel line

Complete Prescribing Information, including Boxed WARNING and Medication Guide, for AVANDIA, AVANDAMET, and AVANDARYL.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase the risk of a myocardial infarction. This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline.
This section is intended for U.S. healthcare professionals only.
© 2011 GlaxoSmithKline. All Rights Reserved.

Avandia-Rosiglitazone Medicines Access Program How Do I Enroll?



IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

LOG IN

Home

Prescribing Information

Medication Guide

For Prescribers:

Only healthcare providers enrolled in the Avandia-Rosiglitazone Medicines Access Program can prescribe rosiglitazone medicines, including:

- Avandia® (rosiglitazone maleate) Tablets,
- Avandamet® (rosiglitazone maleate and metformin hydrochloride) Tablets, and
- Avandaryl® (rosiglitazone maleate and glimepiride) Tablets.

Because of a potential increased risk of myocardial infarction, these medicines are only available through the Avandia-Rosiglitazone Medicines Access Program.

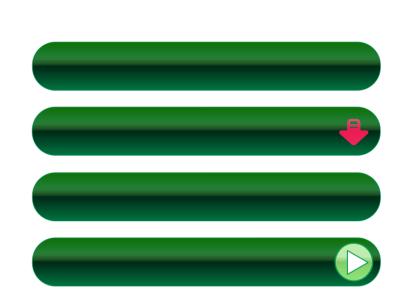
Steps to Prescriber Enrollment

- 1. Review the Prescriber Overview.
- 2. Complete the Prescriber Enrollment Form.
- 3. Submit the Prescriber Enrollment Form to the Coordinating Center either <u>online</u>, <u>over the phone</u>, <u>or by fax</u>.
 - · An enrollment confirmation will be sent to you by e-mail.

You may designate an office contact to assist with communications between your office and the Coordinating Center.

You and your office contact will each receive a username and password to access the web-based system for online patient enrollment.

Once you are enrolled, you can enroll eligible patients into the Avandia-Rosiglitazone Medicines Access Program.



600 pixel line

Complete Prescribing Information, including Boxed WARNING and Medication Guide, for AVANDIA, AVANDAMET, and AVANDARYL.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase the risk of a myocardial infarction. This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline.

This section is intended for U.S. healthcare professionals only.

© 2011 GlaxoSmithKline. All Rights Reserved.

Avandia-Rosiglitazone Medicines Access Program How Do I Enroll a Patient?

Avandia-Rosiglitazone Medicines Access Program™

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

LOG IN

Home

Prescribing Information

Medication Guide

Steps to Enroll a Patient

- 1. Determine that the patient is an appropriate candidate for treatment with rosiglitazone.
- 2. Educate patients on the risks and benefits of taking rosiglitazone, and provide them with a Medication Guide. Encourage them to ask questions about rosiglitazone.
- 3. Answer the questions your patient may have about rosiglitazone and the Avandia-Rosiglitazone Medicines Access Program.
- 4. Review and complete the Patient Enrollment Form with your patient. Be sure that you both sign the form. Be sure to complete the Prescription Information section of the Patient Enrollment Form. Provide the patient with a copy of the signed Patient Enrollment Form.
- 5. Either fax the completed <u>Patient Enrollment Form</u> to the Avandia-Rosiglitazone Medicines Access Program Coordinating Center or log on to the <u>online</u> system and complete the Patient Enrollment Form. Either fax the prescription and insurance information or attach this information as prompted during online enrollment.
- Once the Avandia-Rosiglitazone Medicines Access Program processes the Patient Enrollment Form, the prescription will be submitted to a specially certified mail order pharmacy for dispensing.
- 7. The patient will receive the rosiglitazone medicine by mail from the mail order pharmacy. Rosiglitazone medicines will not be available through retail pharmacies.



600 pixel line

Complete Prescribing Information, including Boxed WARNING and Medication Guide, for AVANDIA, AVANDAMET, and AVANDARYL.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase the risk of a myocardial infarction. This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline.

This section is intended for U.S. healthcare professionals only.

© 2011 GlaxoSmithKline. All Rights Reserved.

Avandia-Rosiglitazone Medicines Access Program Information for Patients

Avandia-Rosiglitazone Medicines Access Program™ IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

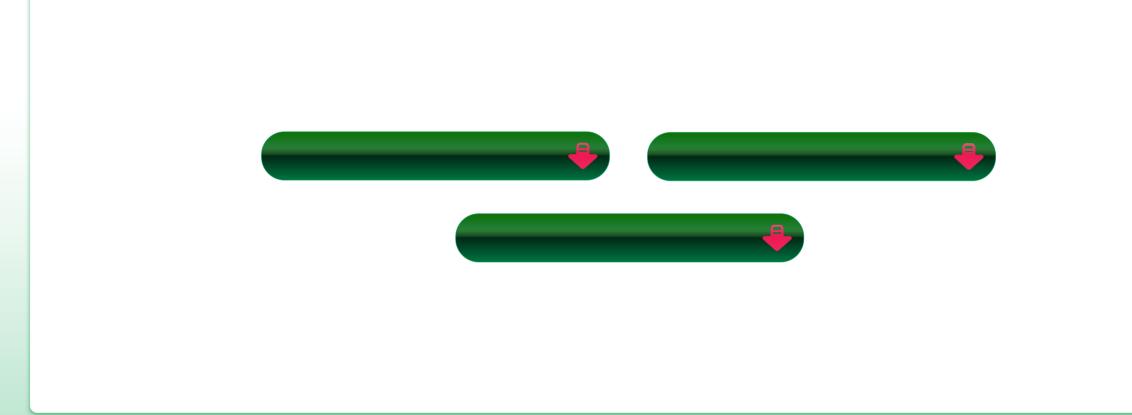
Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

Home

Prescribing Information

Medication Guide



600 pixel line

Complete Prescribing Information, including Boxed WARNING and Medication Guide, for AVANDIA, AVANDAMET, and AVANDARYL.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase your risk of a heart attack (myocardial infarction). This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline.
This section is intended for U.S. residents only.
© 2011 GlaxoSmithKline. All Rights Reserved.

Avandia-Rosiglitazone Medicines Access Program Pharmacist Overview



IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

Home

Prescribing Information

Medication Guide

Under the Avandia-Rosiglitazone Medicines Access Program, there is a restricted access and dispensing system for rosiglitazone medicines.

Rosiglitazone medicines will be withdrawn from supply chains beginning on X date.

Please refer any patients with questions about rosiglitazone medicines or enrollment in the Program to their healthcare provider.

Dear Pharmacist Letter

600 pixel line

Complete Prescribing Information, including Boxed WARNING and Medication Guide, for **AVANDIA**, **AVANDAMET**, and **AVANDARYL**.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase the risk of a myocardial infarction. This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline.

This section is intended for U.S. healthcare professionals only.

© 2011 GlaxoSmithKline. All Rights Reserved.

Avandia-Rosiglitazone Medicines Access Program Coordinating Center



IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

Home

Prescribing Information

Medication Guide

Please call the Coordinating Center with questions about the Avandia-Rosiglitazone Medicines Access Program.

Phone: 1-800-AVANDIA (1-800-282-6342)

Fax: 1-888-772-9404

Avandia-Rosiglitazone Medicines Access Program PO 4649 Star City, WV 26504-4649

Hours of Operation:
Monday through Friday from 8:00 AM to 8:00 PM ET

600 pixel line

Complete Prescribing Information, including Boxed WARNING and Medication Guide, for AVANDIA, AVANDAMET, and AVANDARYL.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase your risk of a heart attack (myocardial infarction). This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline.
This section is intended for U.S. residents only.
© 2011 GlaxoSmithKline. All Rights Reserved.

Welcome to the Avandia-Rosiglitazone Medicines Access Program



IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

SAFETY INFORMATION CONTINUED BELOW

Home Prescribing Information Medication Guide

User Name

Password

LOG IN

Forgot Password?

Login is available only if a username and password has been received from the Avandia-Rosiglitazone Medicines Access Program.

Login is available for enrolled Prescribers, designated Office Contacts and designated Pharmacies only. To learn more about the Avandia-Rosiglitazone Medicines Access Program, please click here.

To enroll in the Avandia-Rosiglitazone Medicines Access Program, you must review the Prescriber Overview.

600 pixel line

Complete Prescribing Information, including Boxed WARNING and Medication Guide, for AVANDIA, AVANDAMET, and AVANDARYL.

IMPORTANT SAFETY INFORMATION about AVANDIA® (rosiglitazone maleate), AVANDAMET® (rosiglitazone maleate/metformin hydrochloride) and AVANDARYL® (rosiglitazone maleate and glimepiride).

AVANDIA, AVANDAMET and AVANDARYL may increase the risk of a myocardial infarction. This risk may be higher in people who are also taking insulin. Because of a potential increased risk of myocardial infarction, AVANDIA, AVANDAMET, and AVANDARYL are available only through the AVANDIA-Rosiglitazone Medicines Access Program.

This is not a complete description of the risks associated with rosiglitazone. Please refer to Boxed Warnings and full Prescribing Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact the Coordinating Center



This website is funded and developed by GlaxoSmithKline. This section is intended for U.S. healthcare professionals only. © 2011 GlaxoSmithKline. All Rights Reserved.

GlaxoSmithKline Internet Privacy Statement GSK respects the privacy of visitors to our online sites. GSK will only collect your

websites.

personally identifiable information, such as your name, address, telephone number, or e-mail address, when you provide it to us at this website. GSK and/or the companies we hire will use this information to comply with your request for information or as otherwise disclosed to you on the web page when you submit your information to us. From time to time, we may refer to this information to better understand your needs and how we can improve our products and services. We may use this information to contact you. We will not sell or otherwise transfer the personally identifiable information you provide to us at this website to any third parties for their own use unless we tell you when you submit your information to us that we intend to do so.

Like many websites, some GSK websites use a technology called "cookies". A

cookie is a small text file that a web server gives your browser to store on your computer when you access a website. Cookies are capable of storing many types of data and may be placed on your browser by GSK or by a third party. Cookies are used for a variety of purposes on GSK websites:

• Some GSK sites set cookies that keep you from having to enter a password

more than once during visits to one or more of our sites.

 We also use cookies to help us analyze usage of our sites and traffic.

among our sites more accurately and to provide you with information of interest to you. For example, cookies are used on some GSK websites to

- Cookies also allow GSK to determine whether you came to a GSK site from another GSK site or from an advertising banner or link on a non-GSK website, so that we can, for example, measure the effectiveness of the links among our sites and the effectiveness of our advertising on non-GSK
- Similarly, cookies allow us to determine whether you register on or visit any
 of our websites, which enables us to analyze how particular users use our
 sites and whether registered and unregistered users of our websites use our
 sites differently.
 Cookies also allow us to maintain information about how particular visitors
- use our family of sites, which enables us to better provide such visitors with information relevant to their interests. This may include using information about your use of our sites in conjunction with personally identifiable information that you have volunteered to us on one of our sites.

 This is not an exhaustive list of all uses of cookies on GSK's websites. In all cases in which cookies are used, however, neither GSK nor any third party will use the

voluntarily agree to enter the information. Most web browsers are set up to accept cookies. You can, however, reset your browser to refuse all cookies or to indicate when a cookie is being sent. Note, however, that some portions of our sites may not work properly if you refuse cookies.

In addition to cookies, GSK may collect non-personally identifiable information about how you use our websites using other analysis technologies. These analysis technologies may be provided by third parties. Information that might be collected using these technologies includes, for example, the pages you visit on our site, the

cookie to collect personally identifiable information from our site unless you

paths you take within our sites and the length of time that you spend on our websites. We use this information in the aggregate in order to better understand

how to improve the quality of our websites.

Some GSK websites use a third party adserving service to display advertising on other, non-GSK websites. In addition to placing advertisements on certain non-GSK web pages, these services and/or GSK may also place a segment of code called a clear pixel tag, also known as a "GIF", on certain GSK web pages that do not contain advertisements for the purpose of measuring the effectiveness of advertisements in bringing visitors to our web sites. GIFs may also be used with cookies to track the total number of visitors to our website, the number of visitors to various web pages, and the domain names of our visitors' Internet service providers. No personally identifiable information is collected in this process.

As is common among Internet site operators, GSK websites maintain web server logs. Web servers automatically identify your computer by its IP address and

collect that information in its web server logs. An IP address is a number that is automatically assigned to your computer by your Internet service provider (e.g., AOL, MSN, Earthlink) whenever you log onto the World Wide Web or "surf" the web. GSK web server logs collect statistical data that is generated by your computer when it visits a GSK website, such as the type of web browser (e.g., Netscape, Internet Explorer) and operating system (Windows 95 or Mac OS) used to access the site, the domain name of your Internet service provider, the date and time you access our site, and the pages you visit. GSK websites use this non-personally identifying web server log information for a variety of purposes. Some of these purposes include: system administration; to examine overall traffic trends on our sites; trouble-shooting; and to gather broad demographic information about users of our sites. No personally identifiable information is contained in these web server logs. This GSK website is not intended or designed to attract children under the age of 13. We do not collect personally identifiable information from any person we know to be under the age of 13.

13. We do not collect personally identifiable information from any person we know to be under the age of 13.
As a convenience to our visitors, GSK's sites currently contain links to a number of websites that we believe may offer useful information. The privacy policy and

provisions described here do not apply to those sites. We suggest contacting those sites directly for information on their data collection and distribution policies.

From time to time, GSK may decide to modify its practices and policies, and we reserve the right to revise this GSK Internet Privacy Statement as necessary to disclose such changes in our practices and policies. Any such changes to this GSK Internet Privacy Statement will be promptly communicated on this page. Any information that you submit before the change in policy will be used by GSK and/or the companies we hire in a manner that is consistent with the GSK Internet Privacy Statement in effect at the time you submitted your information. Continued use of

the companies we hire in a manner that is consistent with the GSK Internet Privacy Statement in effect at the time you submitted your information. Continued use of our sites after receiving notice of a change in our privacy statement shall indicate your consent to the use of newly-submitted information in accordance with the changed, amended, or updated GSK Internet Privacy Statement.

Page 9 of 10

Legal Notices

GlaxoSmithKline offers products and services to diagnose, prevent and treat disease. Its prescription medicines for use by healthcare professionals are regulated by government agencies in each of the countries in which it does business, such as the Food and Drug Administration in the United States (U.S.) or the Committee on Safety of Medicine in the United Kingdom. These regulations often restrict the prescribing information that can be disclosed to the public so that you need to consult with your health care professional. You may also need to visit other healthcare Web sites to find out more about prescription products.

This Web Site has been developed as a service of GlaxoSmithKline. Like any other service, in spite of our best efforts the information in this Web Site may become out of date over time. Nothing on this Web Site should be construed as the giving of advice or the making of a recommendation and it should not be relied on as the basis for any decision or action. It is important that you rely only on the advice of a health care professional to advise you on your specific situation. GlaxoSmithKline accepts no liability for the accuracy or completeness or use of, nor any liability to update, the information contained on this Web Site. These materials are provided "AS IS" WITHOUT WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, THE IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT. Some jurisdictions do not allow the exclusion of implied warranties, so the above exclusion may not apply to you.

Internet, including the Web Sites for GlaxoSmithKline affiliates in other countries. GlaxoSmithKline cannot take responsibility for information found on third party Web sites outside its control. While GlaxoSmithKline attempts to provide links only to third-party Web Sites that comply with all applicable laws and regulations and GlaxoSmithKline's standards, please understand that the content on these third-party Web Sites is subject to change without notice to GlaxoSmithKline. We therefore cannot be responsible for, and accept no liability for, any information or opinion contained in any third-party Web Site.

This U.S.-based Web Site may link you to other Web Sites on the

deal in the securities or ADRs of GlaxoSmithKline. In particular, actual results and developments may be materially different from any forecast, opinion or expectation expressed on this Web Site and the past performance of the price of securities must not be relied on as a guide to their future performance.

Copyright and Intellectual Property

Nothing on this website constitutes an invitation or offer to invest or

GlaxoSmithKline hereby authorizes you to copy materials published

by it on this Web site for non-commercial use only, provided any copy of these materials which you make shall retain all copyright and other proprietary notices and any disclaimer contained thereon and on this Web Site.

Nothing contained herein shall be construed as conferring by

patent or trademark of GlaxoSmithKline or any third party. Except as expressly provided above, nothing contained herein shall be construed as conferring any license or right under any GlaxoSmithKline copyright.

implication, estoppel or otherwise any license or right under any

Trademarks and service marks owned by or licensed to GlaxoSmithKline are presented as italicized typefaces, such as Seretide or Tums. British and American spellings are used, depending on the author or source of the information. GlaxoSmithKline claims no ownership in, nor any affiliation with, any third-party trademarks appearing in this Web Site. Such third-party trademarks are used only to identify the products and services of their respective owners, and no spensorship or endorsement on the

their respective owners, and no sponsorship or endorsement on the part of GlaxoSmithKline should be inferred from the use of these marks.

Should any viewer of a GlaxoSmithKline published document respond with information including feedback data such as questions, comments, suggestions, or the like regarding the content of any such GlaxoSmithKline material, such information shall be deemed to be non-confidential and we shall have no obligation of any kind with respect to such information and shall be free to reproduce use

be non-confidential and we shall have no obligation of any kind with respect to such information and shall be free to reproduce, use, disclose, and distribute the information to others without limitation. We shall be free to use any ideas, concepts, know-how or techniques contained in such information for any purpose whatsoever including but not limited to developing, manufacturing and marketing products incorporating such information.

© 2001-2010 GlaxoSmithKline - All Rights Reserved - Updated January 08, 2001

Done